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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,902	01/25/2001	Reba Goodman	61545/JPW/RAD	5006

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John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 08/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/769,902	GOODMAN ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 July 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-30*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

DAVID T. FOX
PRIMARY EXAMINER

Continuation of 2. NOTE: In the Paper filed after final rejection, the claims have been amended to recite, "providing a gene promoter comprising a 900 base pair segment of c-myc promoter containing nCTCTn electromagnetic field response elements fused to a HSP70 gene promoter heat shock responsive element." In the finally rejected claims, the promoter into which the electromagnetic field response element is inserted was limited to "not having any electromagnetic field response elements". The present claims are not so limited and, therefore, encompass subject matter that was not previously examined. Furthermore, the promoter of the claims is newly limited to comprising a "heat shock responsive element". As this limitation was not present in the previously examined claims, its inclusion in the claims amended after final rejection raises new issues for consideration. Therefore, entry of the amended claims would require additional search and examination and does not simplify the issues for appeal.

Continuation of 3. Applicant's reply has overcome the following rejection(s): Rejection of claims 4, 7, 17, 20, 26 and 29 under 35 U.S.C. 112, first paragraph, as containing new matter is withdrawn. The claims were rejected as lacking descriptive support for identification of a specific region of the HSP70 or c-myc promoter relative to the transcriptional start site. On page 9 of the reply, Applicant cites page 7, lines 12-29 as providing additional support for the amendment. In lines 19-20 on page 7, the specification does in fact identify a promoter region relative to the transcriptional start site and, because the skilled artisan would expect that the benchmark for identifying regions in the genes would be consistent throughout the specification, the teaching provides implicit support for specifying all gene regions relative to the transcriptional start site.

Continuation of 5. does NOT place the application in condition for allowance because: With regard to the rejection of claims 1-12 as lacking enablement under 35 U.S.C. §112, first paragraph, for a method for regulating expression of an exogenous gene introduced into a subject by a gene therapy, Applicant argues that the claims are enabled because gene therapies existed and were known in the art at the time of filing. In support of the assertion that gene therapies were enabled at the time of filing, Applicant cites Tomiyasu et al., Zang et al., Ye et al., and Rosengart et al. as demonstrating in vivo gene therapy. However, as pointed out in previous Office Actions, none of the cited art describes an enabled gene therapy. Tomiyasu et al. teaches, "intra-cardiomuscular transfer of beta2-adrenergic receptor gene in cardomyopathic hamsters significantly elevated stroke volume and cardiac output". However, the improvements shown in cardiac function were small and appeared to be transient (see especially Figure 4). Thus, the findings of Tomiyasu et al. cannot be taken as evidence for clinical efficacy of the method disclosed therein in light of the general unpredictability of the gene therapy technology. Likewise, Zang et al. teaches inhibition of tumor growth in mice bearing an ovarian cancer cell line and provide only speculation that, "this promising procedure could greatly benefit ovarian cancer patients with high expression of HER-2/neu" (abstract). However, there is no evidence that the method disclosed in Zang et al. is a fully enabled gene therapy for any disease. As pointed out in the 16 June 2003 Advisory Action, Ye et al. clearly demonstrates the unpredictability of extending results obtained in one mammalian species to other species of mammals. Experiments performed in mice showed no diminution in induced EPO expression at 6 months after gene transfer (see especially Figures 1 and 2 and the captions thereto), while induced EPO-expression was undetectable in non-human primates 4 months after gene transfer for unknown reasons (see especially Figure 4 and the caption thereto, and the first paragraph in the right column on page 90). Thus, Ye et al. demonstrates the unpredictability of extending positive gene therapy results obtained in mice, such as those described by Zang. Therefore, positive findings in mice are not demonstrative of an enabled gene therapy. Finally, although clinical trial of Rosengart et al. shows some trend toward therapeutic effect, the findings are equivocal due to the small number of patients in the study and, as pointed out by Rosengart et al., "the results are too preliminary to substantiate efficacy" (see especially the first paragraph of the "Discussion" on page 469). Given the high degree of unpredictability regarding obtaining therapeutic efficacy using gene therapy approaches, as established in previous office actions, the skilled artisan would not view the teachings of Rosengart et al. as enabling for a method of gene therapy. Thus, none of the art cited by Applicant can be viewed as teaching an enabled gene therapy and Applicant's arguments are therefore unpersuasive.

The remaining arguments are predicated on entry of the after final amendment. As the amendment has not been entered, these arguments are moot..